

AMENDMENTS TO THE SPECIFICATION

At page 113, after paragraph [0225], please insert the printed Sequence Listing submitted herewith.

Please delete paragraph [0113] on pages 38 and 39 and replace it with the following paragraph. Deletions appear in ~~strike through font~~, and additions are underlined.

[0113] To analyze the effectiveness of substances which bind to human PPAR α , activating it in agonistic manner, a stable transfected HEK cell line (HEK = human emryo kidney) designated here as "PPAR α reporter cell line" is used. It contains two genetic elements, a firefly luciferase reporter element and a PPAR α fusion protein (GR-GAL4-PPAR α) which controls the expression of the firefly luciferase reporter element in a PPAR α ligand dependent way.

The PPAR α reporter cell line was established in two steps: First, the firefly luciferase reporter element was constructed and stably transfected into HEK cells. Five DNA binding sites for the yeast transcription factor GAL4 (five repetitions of the sequence 5'-CGGAGTACTGTCCTCCGAG-3') (SEQ ID NO:1) were cloned 5' upstream of a 68 bp minimal RNA polymerase II promoter from the GR mouse mammary tumor virus long terminal repeat (accession # V01175) providing a CCAAT-box as well as a TATA-element. Cloning and sequencing was done as described by Sambrook J. et. al. (Molecular cloning, Cold Spring Harbor Laboratory Press, 1989). The complete Photinus pyralis luciferase gene (accession # M15077) was cloned 3' downstream of

the GAL4 binding sites and the MMTV minimal promoter. The firefly luciferase reporter element consisting of 5 GAL4 binding sites, the MMTV minimal promoter and the full length luciferase gene was recloned into a plasmid backbone harboring a Zeozin resistance gene leading to plasmid "pdeltaMG4LZ". This vector was transfected in HEK cells as described by Ausubel, F.M. et al. (Current protocols in molecular biology, Vol. 1-3, John Wiley & Sons, Inc., 1995). Stable clones have been selected using Zeozin as a selection agent (0.5 mg/ml).

In a second step, the PPAR α fusion protein (GR-GAL4-PPAR α) that controls expression of the firefly luciferase reporter element, was stably integrated in this cell background. For this purpose the cDNAs coding for the N-terminal 76 amino acids of the human glucocorticoid receptor ("GR", accession # P04150) have been linked to amino acids 1-147 of the yeast GAL4-protein (accession # P04386) followed by the ligand binding domain of human PPAR α (amino acids S167-Y468, accession # S74349). The GR-GAL4-humanPPAR α construct was cloned into plasmid pcDNA3 (Invitrogen) where its expression is driven constitutively by the Cytomegalovirus promoter. The plasmid pcDNA3-GR-GAL4-humanPPAR α was transfected in a stable HEK-cell clone that already contained the firefly luciferase reporter element described above. A double-transfected cell line containing both, the firefly luciferase reporter element as well as the GR-GAL4-humanPPAR α fusion protein, has been selected on medium supplemented with Zeozin (0.5 mg/ml) and G418 (0.5 mg/ml).